The Natural History of Lone Atrial Flutter

Sean C. Halligan, MD; Bernard J. Gersh, MBChB, DPhil; Robert D. Brown Jr., MD; A. Gabriela Rosales, MS; Thomas M. Munger, MD; Win-Kuang Shen, MD; Stephen C. Hammill, MD; and Paul A. Friedman, MD

Background: **The natural history of atrial flutter is not well defined.**

Objective: **To report the risk for stroke, conversion to atrial fibrillation, and anticoagulation for lone atrial flutter.**

Design: **Retrospective cohort analysis.**

Setting: **A clinically based longitudinal study of inpatients and outpatients with atrial flutter.**

Patients: **The authors compared the stroke rate in 59 patients with atrial flutter with rates in a sample in which age- and sex-specific ischemic cerebrovascular event rates were determined and in a sample of nonhypertensive patients with lone atrial fibrillation. The risk for developing atrial fibrillation after presenting with atrial flutter is also reported.**

Measurements: **Electrocardiograms and clinical data were collected and reviewed for each study participant.**

Results: **After adjustment for age and sex, patients with atrial flutter had a higher incidence of thromboembolic events than the sample control patients and patients with atrial fibrillation. Atrial fibrillation developed in 56% of patients with atrial flutter.**

Conclusions: **Lone atrial flutter has a stroke risk at least as high as lone atrial fibrillation and carries a higher risk for subsequent development of atrial fibrillation than in the general population. Anticoagulation should be considered for all patients with atrial flutter who are older than 65 years of age.**

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For author affiliations, see end of text.

The objective of this study was to determine the long-term rate of thromboembolism and the risk for subsequent development of atrial fibrillation in patients who initially presented with lone atrial flutter.

Methods

Between 1965 and 1995, 567 patients from Olmsted County, Minnesota, were seen with atrial flutter. We excluded patients with any of the following conditions at the time of initial presentation: coronary artery disease, hyperthyroidism, valvular heart disease, congestive heart failure, cardiomyopathy, congenital heart disease, obstructive pulmonary disease, uncontrolled hypertension, or antecedent atrial fibrillation. We included patients with a history of controlled hypertension. We also excluded patients who were missing electrocardiographic documentation of atrial flutter, who had life-shortening disease, or whose atrial flutter occurred only as a consequence of an acute illness. Two physicians reviewed electrocardiograms to confirm the diagnosis. Atrial flutter was defined as a regular monomorphic rhythm with atrial rate greater than 240 beats/min and less than 350 beats/min. The Mayo Institutional Review Board, Rochester, Minnesota, approved the study.

Control Groups

The first control group was a previously defined sample in Rochester, Minnesota, in which age- and sex-specific ischemic cerebrovascular event rates were determined for the period of 1965 to 1994 (referred to as the *incident cohort*). The second control group consisted of Olmsted County patients who had no history of hypertension and received a diagnosis of lone atrial fibrillation from 1950 to 1980 (1, 2).

Statistical Analysis

Continuous variables were summarized as means ± 1 SD, and categorical variables were summarized as percentages. Survival without atrial fibrillation or stroke or transient ischemic attack was estimated by using the Kaplan–Meier method, and comparisons between patient groups were based on the log-rank test. The standardized stroke or transient ischemic attack rates were defined as the ratio of observed strokes or transient ischemic attacks in the patient cohorts divided by the expected number of strokes or transient ischemic attacks when applying the age- and sex-specific rates obtained from the incident cohort. The estimated rate of survival without stroke is expressed as the ratio of observed rates to the age- and sex-adjusted expected rates.

Cox proportional hazards techniques were used to identify variables associated with rates of survival without atrial fibrillation and survival without stroke or transient ischemic attack. Because of the small numbers of events, the multivariate models consisted of only 3 variables: age; sex; and 1 of the following: body mass index, ejection fraction, duration of first atrial flutter episode (dichotomized as $<$24 hours or $\geq$24 hours), diabetes, history of cerebrovascular event, history of hypertension, and symptoms. All tests were 2-tailed, and a P value of 0.05 was the level of significance.

Follow-up continued until January 2001 or death. A neurologist adjudicated all cerebrovascular events.

Role of the Funding Source

This study was funded through a grant from Mayo Foundation, which had no role in the collection, analysis, or interpretation of the data or in the decision to publish the manuscript.

Context

While the adverse consequences of atrial fibrillation have received much attention, we know little about the outcomes of people with lone atrial flutter.

Contribution

Among 59 patients with lone atrial flutter cared for at the Mayo Clinic between 1965 and 1995, 33 developed atrial fibrillation and 19 sustained a cerebrovascular event over an average follow-up of 10 years. The rate of thromboembolic events observed in this sample of patients with lone atrial flutter was at least as high as that observed in patients with atrial fibrillation.

Cautions

This observational study cannot tell us whether treatment for atrial flutter and anticoagulation would improve outcomes for people with lone atrial flutter.

–The Editors

Results

Fifty-nine patients developed lone atrial flutter during the 30-year period (**Table**); 75% developed recurrent episodes or chronic flutter. The average age at diagnosis was 70 years (range, 40 to 97 years). No patient with atrial flutter had clinically evident heart disease at the time of initial diagnosis. However, 20 patients had controlled hypertension, 11 had diabetes mellitus, 3 had had a transient ischemic attack (2 years, 6 years, and 10 years before diagnosis of atrial flutter, respectively), and 1 had had an ischemic stroke (9 years before diagnosis of atrial flutter). The clinical characteristics of the patients with controlled hypertension and atrial flutter did not statistically significantly differ from those of the nonhypertensive patients with atrial flutter.

Table. **Characteristics of Patients with Lone Atrial Flutter***

Characteristic	Value
Sex, *n*	
Men	33
Women	26
Age at diagnosis, *y*	70 ± 12
Age range, *n*	
40–50 y	4
51–60 y	5
61–70 y	19
71–80 y	18
81–90 y	12
91–100 y	1
Body mass index, kg/m^2†	26 ± 5
Left ventricular ejection fraction‡	0.55 ± 0.13
First flutter episode duration < 24 h, *n*§	10
Duration of follow-up, *y*	10 ± 6
History, *n*	
Hypertension (controlled)	20
Diabetes mellitus	11
Ischemic stroke	1
Transient ischemic attack	3
Symptoms, %‖	
At least one symptom	96
Palpitations	56
Shortness of breath or dyspnea on exertion	44
Dizziness	25
Chest pain	19
Fatigue	13
Syncope	10

* Values expressed with a plus/minus sign are means ± SD.
† Available for only 57 patients.
‡ Available for only 36 patients.
§ Available for only 55 patients.
‖ Available for only 48 patients.

Medical therapy was started in 88% of patients: digitalis (61%), β-blockers (17%), calcium-channel blockers (31%), and antiarrhythmic drugs (24%). Four patients underwent atrial flutter ablation.

At the time of diagnosis, 31 patients received antithrombotic or antiplatelet therapy (25 patients received aspirin, and 6 patients received warfarin) to prevent embolic events. The other patients did not receive any antithrombotic or antiplatelet therapy. At latest follow-up, 41 patients were being treated with antithrombotic or antiplatelet agents (28 patients received aspirin, and 13 patients received warfarin) to prevent embolic events.

Subsequent Development of Atrial Fibrillation

Atrial fibrillation developed in 33 patients (paroxysmal in 25 patients and chronic in 8 patients). The average (±SD) time from atrial flutter diagnosis to atrial fibrillation was 5 ± 6 years (range, 0 to 25 years) (**Figure**). Unadjusted associations for the risk for atrial fibrillation were female sex (hazard ratio, 2.0 [95% CI, 0.95 to 4.2]; $P = 0.07$), diabetes (hazard ratio, 2.6 [CI, 1.1 to 6.0]; $P = 0.028$), hypertension (hazard ratio, 2.9 [CI, 1.4 to 6.1]; $P = 0.005$), recurrent atrial flutter (hazard ratio, 2.6 [CI, 0.91 to 7.6]; $P = 0.074$), and older age at the time of diagnosis of atrial flutter (hazard ratio, 1.05 [CI, 1.01 to 1.08]; $P = 0.007$). Significant age- and sex-adjusted predictors for developing atrial fibrillation were diabetes (hazard ratio, 2.7 [CI, 1.1 to 6.4]; $P = 0.029$), hypertension (hazard ratio, 2.4 [CI, 1.2 to 5.1]; $P = 0.02$), and recurrent atrial flutter (hazard ratio, 3.1 [CI, 1.03 to 9.1]; $P = 0.044$).

Cerebrovascular Events

Nineteen patients, with a mean (±SD) age of 80 ± 10 years, experienced at least 1 cerebrovascular ischemic event during follow-up. The mean (±SD) time from atrial flutter diagnosis to cerebrovascular event was 4.3 ± 3.9 years. Of the 19 patients, 6 developed atrial fibrillation after the atrial flutter diagnosis but before the event. Of the 4 patients with a history of stroke or transient ischemic attack before the atrial flutter diagnosis, only 1 patient had a cerebrovascular event during follow-up.

Among patients with atrial flutter, 77% were free of ischemic stroke or transient ischemic attack, whichever occurred first, at 5 years and 65% were free of one of these events at 10 years. Among the incident cohort, 94% at 5 years and 89% at 10 years were free of one of these events

(standardized stroke or transient ischemic attack rate, 3.3 [CI, 2.1 to 5.2]; $P < 0.001$). Patients with controlled hypertension and atrial flutter had an estimated 5- and 10-year survival rate without cerebrovascular events of 70% and 52%, respectively, as compared with 80% and 75% for nonhypertensive patients, respectively (log-rank $P = 0.099$), with an age- and sex-adjusted hazard ratio of 2.3 (CI, 0.87 to 6.0; $P = 0.094$). However, both the patients with controlled hypertension and atrial flutter and nonhypertensive patients with atrial flutter had statistically significant higher rates of stroke or transient ischemic attack than the incident cohort (standardized stroke or transient ischemic attack rate, 5.2 [CI, 2.7 to 9.9; $P < 0.001$] and 2.5 [CI, 1.3 to 4.6; $P = 0.002$], respectively).

Comparison with Patients with Lone Atrial Fibrillation

Data from the 59 patients with atrial flutter were compared with those from 145 patients with atrial fibrillation. The atrial flutter group had a larger percentage of women (44% vs. 28%; $P = 0.04$), was older on average (70 ± 12 years of age vs. 55 ± 17 years of age; $P < 0.001$), and had less follow-up time on average (10 ± 6 years vs. 13 ± 8 years; $P = 0.002$) than the atrial fibrillation group. Also, the atrial fibrillation group excluded patients with a history of hypertension before their diagnosis. After adjustment for age and sex, patients with atrial flutter had a higher incidence of ischemic stroke or transient ischemic attack than patients with atrial fibrillation (hazard ratio, 2.6 [CI, 1.2 to 5.3]; $P = 0.011$). Moreover, when nonhypertensive patients with atrial flutter were compared with patients with atrial fibrillation, the rate of stroke or transient ischemic attack did not differ (hazard ratio, 1.9 [CI, 0.85 to 4.4]; $P = 0.119$).

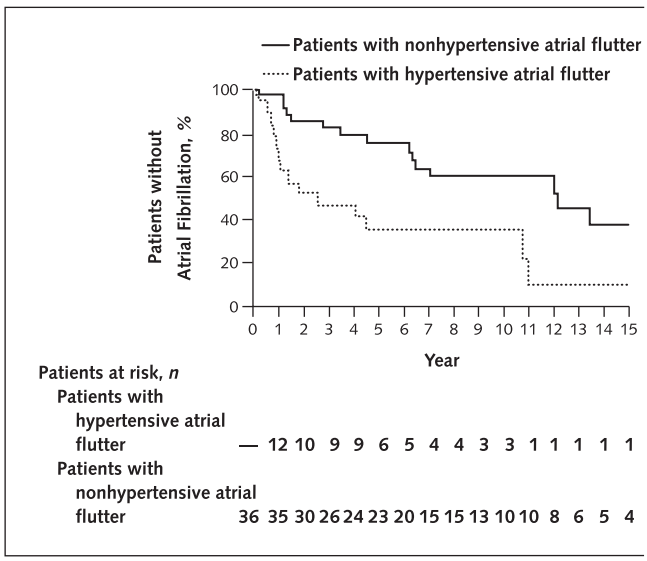
Discussion

In our study, 32% of patients with atrial flutter had a cerebrovascular event at 10-year follow-up. Compared with the age- and sex-adjusted expected thromboembolic rates, patients with atrial flutter experienced a statistically higher risk. Also, the rate of thromboembolism was higher in the patients with atrial flutter than in patients with atrial fibrillation. This observation, in part, is probably due to inclusion of patients with controlled hypertension in the atrial flutter group. However, when nonhypertensive patients with atrial flutter were compared with the incident cohort, there was a higher incidence of thromboembolic events in patients with atrial flutter. This suggests that atrial flutter, even without hypertension, carries a risk similar to that of lone atrial fibrillation and patients with atrial flutter and controlled hypertension are at even higher risk for thromboembolic events.

Atrial Flutter and Subsequent Atrial Fibrillation

Most patients with atrial flutter (56%) developed atrial fibrillation within a mean (±SD) of 5 ± 6 years, similar to previous reports (3). Moreover, because atrial fibrillation frequently is asymptomatic (4), the number of patients with atrial flutter and subsequent atrial fibrillation was probably underestimated. The finding that advanced age, female sex, diabetes, and hypertension seem to predispose patients with atrial flutter to atrial fibrillation is striking because these are known risk factors for thromboembolism in atrial fibrillation (5).

Figure. **Kaplan–Meier curves depict the time without conversion to atrial fibrillation from the initial lone atrial flutter diagnosis.**



Although catheter ablation is an effective treatment for atrial flutter and has become common (6), it is unclear whether ablation will decrease the risk for future atrial fibrillation. Therefore, patients undergoing atrial flutter ablation should continue to be evaluated to exclude the development of fibrillation.

Limitations

Our observations and conclusions should be interpreted in the light of the limitations imposed by the study design. Selection of study patients was not random, but the inclusion of consecutive patients minimized selection bias. We cannot exclude covert coronary disease in such an elderly sample. We also included patients with controlled hypertension and diabetes. Although the total number of patients was small, follow-up was long.

Conclusions

Patients with lone atrial flutter have an increased risk for thromboembolism. These findings support the use of anticoagulation for all patients with atrial flutter who are older than 65 years of age. Atrial fibrillation develops in most patients with atrial flutter. Further studies are needed to determine whether catheter ablation alters the high rate of subsequent atrial fibrillation.

From the Mayo Clinic, Rochester, Minnesota.

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Corresponding Author: Paul A. Friedman, MD, Division of Cardiovascular Diseases and Internal Medicine, Mayo Clinic, 200 First Street SW, Rochester, MN 55905.

Current author addresses and author contributions are available at www.annals.org.

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Current Author Addresses: Drs. Halligan, Brown, Munger, Shen, Hammill, Friedman, and Gersh and Ms. Rosales: Mayo Clinic, 200 First Street SW, Rochester, MN 55905.

Author Contributions: Conception and design: S.C. Halligan, B.J. Gersh, R.D. Brown Jr., T.M. Munger, S.C. Hammill, P.A. Friedman.
Analysis and interpretation of the data: S.C. Halligan, B.J. Gersh, R.D. Brown Jr, A.G. Rosales, T.M. Munger, S.C. Hammill, P.A. Friedman.
Drafting of the article: S.C. Halligan, B.J. Gersh, R.D. Brown Jr., S.C. Hammill,
Critical revision of the article for important intellectual content: S.C. Halligan, B.J. Gersh, R.D. Brown Jr., A.G. Rosales, W.-K. Shen, S.C. Hammill, P.A. Friedman.
Final approval of the article: B.J. Gersh, R.D. Brown Jr., T.M. Munger, W.-K. Shen, S.C. Hammill, P.A. Friedman.
Provision of study materials or patients: S.C. Halligan.
Statistical expertise: A.G. Rosales.
Obtaining of funding: S.C. Halligan.
Administrative, technical, or logistic support: R.D. Brown Jr., S.C. Hammill, P.A. Friedman.
Collection and assembly of data: S.C. Halligan.